REMARKS

Status of the Claims.

Claims 70 and 87 are pending with entry of this amendment, claims 1-69, and 71-86 being canceled and claim 87 being added herein.

Title of the Invention.

The Examiner required a new title that is clearly indicative of the invention to which the claims are directed. The title is amended herein thereby obviating this rejection.

Election/Restriction.

Pursuant to a restriction requirement made final, Applicants cancel claims 1-69, and 71-86 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancelations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Information Disclosure Statement.

Applicants submit herewith a supplemental Information Disclosure Statement (IDS). Applicants request that the references on the IDS be expressly considered during the prosecution of this application and the references be made of record therein and appear among the "references "cited on any patent to issue therefrom.

Statutory Double Patenting.

Claim 70 was provisionally rejected under 35 U.S.C. §101 as allegedly claiming the same invention as that of claim 27 of copending Application No: 10/111,727. It is noted that this is a **provisional** double patenting rejection since the conflicting claims have not, in fact been patented. Accordingly no action is required at this time.

35 U.S.C. §101

Claim 70 was rejected under 35 U.S.C. §101 because the claimed invention allegedly lacked patentable utility. In particular, the Examiner allegedly that the specification does not provide data to confirm that MARPs play a role in treating a wasting syndrome and therefore lacks a specific, substantial, and credible utility. Applicants traverse.

The presently pending claims are directed to MARP-33, a "Minimized Agouti Related Protein) or to formulations comprising such a protein. It is well recognized that the full length Agouti-Related Protein (AGRP) is effective in stimulating food intake (hence in treating a wasting condition). As stated by Fakete *et al.*:

> Agouti-related protein (AGRP) is thought to be one of the neuropeptides mediating the effects of leptin on appetite and satiety. **The central administration of AGRP not only stimulates food intake, but also inhibits the hypothalamic-pituitary-thyroid axis (HPT)axis, closely replicating the central hypothyroid state induced by fasting.** [Emphasis added} (Fekete *et al.* (2004) *Endocrinology*, online publication: doi:10.1210/en.2004-0476, reference 22 in accompanying IDS)

The presently claimed MARP-33 corresponds to residues 87-120 of AGRP. It is well established that MCR activity of AGRP is localized to these residues. As stated by Jackson *et al.* (2002) *Biochemistry*, 41: 7565-7572 (reference 24 in accompanying IDS):

> The agouti-related protein (AGRP) is an endogenous antagonist of the melanocortin receptors MC3R and MC4R found in the hypothalamus and exhibits potent orexigenic activity. **The cysteine-rich C-terminal domain of this protein, corresponding to AGRP (87-132), exhibits receptor binding affinity and anatagonism equivalent to that of the full-length protein.** [emphasis added] (see Jackson *et al.* abstract)
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> The designed mini-protein [MARP-33 a.k.a. AGRP(87-120)] folds to a homogeneous product, retains the desired cysteine knot architecture, **functions as an antagonist, and maintains the melanocortin receptor pharmacological profile of AGRP(87-132)**. [emphasis added] (see Jackson *et al.* abstract)
>
> It is noted that AGRP(87-132) is as active as the full-length agouti protein:
>
> While full length agouti and AGRP are only 25% homologous, in their 46 residue Cys-rich C-terminal regions nine of the 10 Cys residues are spatially conserved and there are a further 10 identical residues giving ~40% sequence identity. Three consecutive, conserved residues RFF (111-113 in human AGRP) were determined to be essential to the biological activity of both agouti [8,9] and AGRP [10]**. Two recent investigations have shown that the chemically synthesized C-terminal region of AGRP competitively**

> **antagonizes α-melanocyte stimulating hormone (α-MSH) at melanocortin receptors with equal or greater potency than the full proteins [11,12], consistent with similar findings for agouti [13]**. [emphasis added] (Bolin *et al.* (1999) *FEBS Letts.*, 451: 125-131, reference 4 in IDS submitted on April 19, 2002 in previous IDS)

The prevailing scientific literature thus clearly establishes that the presently claimed MARP-33 has the same pharmacological profile and activity as the AGRP(87-132) and the full-length agouti protein. Moreover, it is establilhsed that central administration of AGRP (and thus MARP-33) stimulates food intake (*e.g.*, stimulates appetite). Thus, the presently claimed invention has specific, substantial, and credible utility (*e.g.*, stimulation of appetite and/or treatment of wasting conditions). Accordingly, the rejection under 35 U.S.C. §101 should be withdrawn.

35 U.S.C. §112, First Paragraph.

Claim 70 was rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. In particular, the Examiner alleged that because "it appears speculative whether the polypeptide of SEQ ID NO: 3 plays a role in any of the asserted utilities as described above in the 35 U.S.C. §101 rejection", it would require undue experimentation to determine the activity or property of the peptide such that it can be determined how to use the claimed sequence. Applicants traverse.

As stated above, the prevailing scientific literature clearly establishes that the presently claimed MARP-33 has the same pharmacological profile and activity as the AGRP(87-132) and the full-length agouti protein. Moreover, it is established that central administration of AGRP (and thus MARP-33) stimulates food intake (*e.g.* stimulates appetite).

Accordingly, a specific, substantial and credible utility has been established and no undue experimentation is required to determine the activity or property of the peptide. The requirements of 35 U.S.C. §112, first paragraph, are fully met and the rejection of claim 70 on these grounds should be withdrawn.

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 769-3513.

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Respectfully submitted,

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